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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of)
)
ROSENBERG et al.)
)
PCT/EP2003/011205)
)
Serial No. 10/530,483)
)
Filing or 371(c) Date: April 6, 2005)
)

For: METHOD FOR PRODUCING SOLID GALENIC FORMULATIONS USING A CROSSLINKED NON-THERMOPLASTIC CARRIER

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Signature: J. D. Voight

Honorable Commissioner for Patents
Alexandria, Virginia 22313-1450

SUBMISSION OF ENGLISH TRANSLATION OF PAPER

Please enter the enclosed English Translation of the International Preliminary Examination Report in the above-reference application.

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Respectfully submitted,
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PATENT COOPERATION TREATY

PCT/EP2003/011205

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M742135-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2003/011205	International filing date (*day/month/year*) 09 October 2003 (09.10.2003)	Priority date (*day/month/year*) 09 October 2002 (09.10.2002)
International Patent Classification (IPC) or national classification and IPC A61K 9/16		
Applicant ABBOTT GMBH & CO. KG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 27 April 2004 (27.04.2004)	Date of completion of this report 28 January 2005 (28.01.2005)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

Form PCT/IPEA/409 (cover sheet) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/011205

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-13 , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:

pages 1-9 , as originally filed
pages _____ , as amended (together with any statement under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the drawings:

pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☐ the sequence listing part of the description:

pages _____ , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

Form PCT/IPEA/409 (Box I) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11205

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims	1-9	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

2. Citations and explanations

The documents are numbered in the same sequence in which they appear in the search report.

D1 describes a method of producing stable granules. At 30°C, 13.2 % omeprazole, 66.6 % crosslinked polyvinyl-pyrrolidone (Kollidon ® CL-M), 6.6 % polyalkoxylated glycerides (Gelucire ®) and 13.2 % Akomed R are mixed and allowed to cool (see example 6). In comparison with the differently composed formulations of examples 1 to 5, the formulation of example 6 displays far quicker release of the active substance (see table 8).

D2 discloses a process for producing a stable and rapid-release formulation, wherein the components are mixed at 150°C and then cooled immediately. The mixture contains 32.6 % itraconazole, 48.9 % hydroxypropylmethylcellulose (HPMC), 13 % Na-croscamellose and 5.5 % glycerol mono-stearate (see example 6).

In **D3** the components of a mixture (*inter alia* 66 % carbochromene-HCl, 7.4 % wax and 2.9 % sodium carboxy-methyl cellulose) are mixed at 70°C or 90°C, cooled and compressed with further adjuvants to form tablets (see

examples 3 and 5).

In **D4** a mixture of 20 % active substance, 20 % crospovidone and 40 % HPMC is melted at 185°C, cooled to room temperature and further processed to produce forms of medicaments, such as tablets (see example 10 and paragraph [0036]).

1. Novelty

The subject matter of claims 1 to 9 appears to be novel within the meaning of PCT Article 33(2) in light of the available documents.

2. Inventive step

The subject matter of claims 1 to 9 involves an inventive step within the meaning of PCT Article 33(3).

The problem addressed by the present invention is the devising of alternative processes for producing a dosage form which rapidly releases poorly soluble active substances.

The proposed solution to the problem is a process which involves mixing 50 to 99.4 % of a cross-linked, non-thermoplastic excipient, 0.5 to 30 % of a thermoplastic adjuvant and 0.1 to 49.5 % of an active substance at temperatures of at least 70°C and then cooling.

D2 represents the closest prior art. It describes a process for producing a stable, rapid-release formulation in which the components are mixed at 150°C and then cooled immediately. The mixture

contains 32.6 % itraconazole (active substance), 48.9 % hydroxypropylmethylcellulose (HPMC; thermoplastic polymer), 13 % sodium croscarmellose (cross-linked, non-thermoplastic excipient) and 5.5 glycerolmonostearate (see example 6).

D1 discloses the production of stable granules having the composition claimed in claim 1 of the present application (see example 6) The method steps involve the mixing of the components at 60°C or 30°C and then cooling the compound.

Since example 6 of D1 displays considerably faster release of the active substance than the other formulations in that document (see table 8), a person skilled in the art would be prompted to select this composition for producing a rapid-release dosage form. However, he would have no reason to carry out the production process at higher temperatures, as with the D2 to D4 processes.

Therefore the subject matter of claims 1 to 9 involves an inventive step.

3. Industrial applicability

The subject matter of claims 1 to 9 has industrial applicability within the meaning of PCT Article 33(4).